REMARKS

New Matter

The Examiner stated that the newly introduced limitation of "non-immortalized" in Claim 42 raises a new matter issue. 1/23/09 Advisory Action at 2. Applicants respectfully disagree with Examiner that the "non-immortalized" limitation is new matter.

As the Examiner is well aware, the Application is directed to a composite containing retinal pigment epithelial (RPE) and RPE equivalent cells, which are primary, i.e., non-immortalized, cells derived from the retina, iris, ciliary body, adult stem cells or embryonic stem cells. *See* Application at [0003], [0053].

The examples in the Application were also performed using primary, non-immortalized RPE cells harvested from normal rabbit tissue. *See, e.g.*, [0095]. The Examiner even recognizes that RPE cells harvested from normal tissue (such as those disclosed in the present Application) are "non-immortalized RPE cells." 1/23/09 Advisory Action at 2. Therefore, there is ample support in the original Application for the claim limitation "non-immortalized." The limitation "non-immortalized" in Claim 42 simply expresses that the RPE cells and RPE equivalent cells in the claim do not include immortalized cells, such as those cells described in [0055]. The limitation does not add new matter. Applicants respectfully request that the Examiner withdraw the new matter rejection.

Overcome Rejections

Applicants thank the Examiner for withdrawing the claim rejections under 35 U.S.C. § 102 based on Young et al., and under § 103 based on Dutt et al. once the amendment is entered. Advisory Action at 2. To clarify, the only remaining rejection is the rejection under 35 U.S.C. § 103 based on Young et al. and supporting references.

Remaining Rejection – 35 U.S.C. § 103 based on Young et al.

The Examiner stated that there is no clear evidence to prove the unexpected result of the present Application that 16,000 to about 20,000 non-immortalized RPE or RPE equivalent cells per 4 mm^2 of amniotic membrane can be seeded and grown directly on the amniotic membrane without having to be transferred as an epithelial monolayer sheet. Advisory Action at 2. Applicants respectfully disagree that the Application does not demonstrate this unexpected result over Young et al.

Notably, the Examiner agrees that Young et al. uses an *intact* epithelium, based on the finding that RPE in suspension do not form an intact monolayer and have not been shown to be beneficial in the treatment of human disease. *Id.* The Examiner further agrees that Young et al. states that an intact epithelium/monolayer is required. *Id.*

The Examiner states that one of ordinary skill in the art could use RPE cells in suspension to cover the entire surface of the amniotic membrane to form a complete monolayer to mimic the intact epithelium. Advisory Action at 2. Although it is feasible for one of ordinary skill in the art to use RPE cells in suspension to cover a known area, the Examiner critically fails to cite to a reason why one of skill in the art would be motivated to cover an amniotic membrane with RPE cells in suspension when Young et al. disclose that "RPE in suspension . . . . have not been shown to be beneficial in the treatment of human disease." *See id.*

Recall that the claims are directed to a 'method for treating a retinal disease, comprising inserting in a subretinal space of a patient in need thereof.' Young et al state that RPE in suspension are not useful for treating human diseases: based on the teachings of Young et al, a person of skill in the art would avoid inserting such cells into the eye of a patient in need. Applicants respectfully urge the Examiner to not divorce the claimed use of the invention with a hypothetical (and non-medical) extension of Young et al.

Further, the Examiner does not cite to any reason why one of skill in the art would use RPE cells in suspension to mimic the intact epithelium, when Young expressly teaches (and the Examiner agrees with) that RPE cells should be harvested as a sheet and that the layer should not be disturbed

from its native apposition when delivered onto a supporting membrane. Young et al. at 14. The only reason Examiner appears to cite is that one of skill in the art "could" cover a known area with a suspension of cells. But why do this in the context of a medical therapy when Young et al teach the ineffectiveness of such cells to treat human diseases. Again, the context of the instant claims (medical therapy; implant into eye) further distinguishes the instant claims from the art.

Thus, one of Applicant's theses is that one of skill in the art would not choose to optimize the number of RPE cells in suspension on amniotic membrane when the art provides no motivation to, and expressly teaches away from doing so (especially in the context of treating human diseases and inserting the composite into a human eye. Therefore, Young et al. and supporting references do not render the claims of the instant application obvious. Applicants respectfully request that the Examiner withdraw the final § 103 rejection over Young et al., and submit that the pending amendments place the application in a condition for allowance. Applicants would be happy to discuss any of the above with Examiner should the Examiner wish to further clarify any of the above points.

CONCLUSION

Applicants submit that this paper fully addresses the Final Office Action mailed October 28, 2008 and the Advisory Action mailed January 23, 2009. Applicants respectfully solicit the Examiner to expedite the prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned attorney at (858) 350-2306. The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit account No. 23-2415 (Attorney Docket No. 34157-707.831).

Respectfully submitted,

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Date: February 25, 2009 By: _____

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